OVERVIEW
This policy documents the coverage of the genetic assays test for RET mutations in detecting the presence of medullary carcinoma of the thyroid and to stop its progression to the lymph nodes.

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
Commercial products:

Genetic testing for germline mutations of the RET proto-oncogene in medullary carcinoma of the thyroid mutations is covered.

BlueCHiP for Medicare:
Medicare excludes all screening (not just genetic screening) with certain statutory exceptions. Blue CHiP for Medicare provides no additional benefits for genetic screening. Only if the patient exhibits signs or symptoms of the disease would the test not be considered screening.

MEDICAL CRITERIA
None

BACKGROUND
Medullary carcinoma of the thyroid is an uncommon type of thyroid cancer that arises from the parafollicular or C cells thyroid, which produces the hormone calcitonin. (Papillary thyroid cancer, arising from the glandular cells, is the most common type of thyroid cancer.) Three distinct but related familial cancer syndromes together are responsible for approximately one-fourth of the incidence of medullary carcinoma of the thyroid; the remaining three-fourths are sporadic. The three inherited syndromes include multiple endocrine neoplasia (MEN) types 2A and 2B and familial medullary thyroid cancer (FMTC). MEN 2A and MEN 2B differ from each other (and from MEN 1) in the spectrum and frequency of accompanying endocrine malignancies and other disorders. In contrast, FMTC is defined as being in a family with the repeated occurrence of medullary thyroid cancer in the absence of other endocrine malignancies or disorders. MEN 2A, MEN 2B, and FMTC are all dominantly inherited. Point mutations of the germline ret proto-oncogene or RET gene, located on chromosome 10, are associated with inheritance of MEN 2A, MEN 2B, or FMTC.

Medullary thyroid cancer is curable surgically if detected before it has spread to regional lymph nodes. However, lymph node involvement at diagnosis may be found in up to 75% of patients for whom a thyroid nodule is the first sign of disease. Surveillance by annual biochemical monitoring has been used to identify those with the inherited disease before it progresses beyond the earliest stages. The development of invasive medullary thyroid cancer usually is preceded by C-cell hyperplasia, which can be detected by hypersecretion of calcitonin in response to a chemical challenge.
Recently, genetic assays for RET mutations have been used as an alternative to annual biochemical testing for C-cell hyperplasia, in patients with a known family history of MEN 2A, 2B, or FMTC. Annual biochemical screening can be stopped in those patients who test negative for mutations. Patients who test positive may undergo immediate thyroidectomy or postpone thyroidectomy until biochemical tests suggest evolving medullary cancer. Genetic assays have also been used to determine if new cases of medullary thyroid cancer without a family history are truly sporadic in origin. A positive test in this setting should initiate evaluation of family members. In addition, a positive test may prompt screening for pheochromocytoma, a component of MEN 2A and 2B, in the affected patient.

Genetic testing for RET proto-oncogene point mutations are generally found among:
- Members of families with defined RET gene mutations;
- Members of families known to be affected by inherited medullary thyroid cancer, but not previously evaluated for RET mutations; and
- Patients with sporadic medullary thyroid cancer.

**COVERAGE**
Benefits may vary between groups/contracts. Please refer to the Evidence of Coverage or Subscriber Agreement, or Benefit Booklet for applicable genetic testing coverage.

**CODING**
CPT codes for genetic testing are not specific to the purpose for the test (e.g. for a tumor marker are compared to screening). Genetic testing code modifiers (CPT Appendix I) do provide disease state specificity in some cases and should be used.

Note: Claims submitted using molecular diagnostic CPT codes are covered services. Claims submitted by proprietary test name (without codes) may be subject to review.

**HCPCS**
S3840 DNA analysis for germline mutations of the RET proto-oncogene for susceptibility to multiple endocrine neoplasia type 2.

**RELATED POLICIES**

<table>
<thead>
<tr>
<th>Published</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provider Update</td>
<td>Feb 2013</td>
</tr>
<tr>
<td>Provider Update</td>
<td>Mar 2012</td>
</tr>
<tr>
<td>Provider Update</td>
<td>Jan 2010</td>
</tr>
<tr>
<td>Provider Update</td>
<td>Nov 2009</td>
</tr>
<tr>
<td>Policy Update</td>
<td>Jan 2008</td>
</tr>
<tr>
<td>Policy Update</td>
<td>Nov 2008</td>
</tr>
<tr>
<td>Policy Update</td>
<td>Aug 2006</td>
</tr>
<tr>
<td>Policy Update</td>
<td>Jul 2001</td>
</tr>
</tbody>
</table>

**REFERENCES**
This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.